

10

=> s fibrate or fenofibrate

31 FIBRATE
90 FENOFIBRATE
L1 114 FIBRATE OR FENOFIBRATE

=> s l1 and 514/937/cclst

773 514/937/CCLST
L2 1 L1 AND 514/937/CCLST

=> d 1

1. 5,645,856, Jul. 8, 1997, Delivery systems for hydrophobic drugs;
Jonathan Ernest Lacy, et al., 424/455, 456; 514/784, 785, 786, **937**,
975 [IMAGE AVAILABLE]

=> d kwic

US PAT NO: 5,645,856 [IMAGE AVAILABLE] L2: 1 of 1
US-CL-CURRENT: 424/455, 456; 514/784, 785, 786, **937**, 975

DRAWING DESC:

DRWD(106)

Lipid regulating agents: bezafibrate, clofibrate, **fenofibrate**,
gemfibrozil, probucol.

DRAWING DESC:

DRWD(121)

In . . . much higher solubilising power for hydrophobic drugs
than
pure bile salt micelies. This is illustrated with the hydrophobic
antihyperlipoproteinemic drug **fenofibrate** which we have shown is
>20
times more soluble in mixed micelles than simple bile salt
micelies.

DETDESC:

DETD(30)

The drugs investigated using this method were: Carbamazepine,

.griseofulvin, **fenofibrate** and probucol.

DETDESC:

DETD(33)

Solubility (Relative to Buffer)

Experiment

Carbamazepine

Griseofulvin

Fenofibrate

Probucol

i	1	1	1	1*
ii	1.1	4.6	38.5	>71.0
iii	2.6	7.4	188.5	>320.0
iv	2.7.	.	.	.

DETDESC:

DETD(57)

80

275 mg
Priolene 275 mg
Soybean Oil
185 mg
Triacetin
185 mg
Fenofibrate
80 mg

=> s 11 and 514/938/cclst

620 514/938/CCLST
L3 0 L1 AND 514/938/CCLST

> s l1 and (caprylic? or capric? or lauric?)

6003 CAPRYLIC?

6083 CAPRIC?

14507 LAURIC?

L4 5 L1 AND (CAPRYLIC? OR CAPRIC? OR LAURIC?)

=> d 1-5

1. 5,786,344, Jul. 28, 1998, Camptothecin drug combinations and methods with reduced side effects; Mark J. Ratain, et al., 514/100, 211 [IMAGE AVAILABLE]

2. 5,719,197, Feb. 17, 1998, Compositions and methods for topical administration of pharmaceutically active agents; David P. Kanios, et al., 514/772.6; 424/435, 443; 514/781, 782 [IMAGE AVAILABLE]

3. 5,645,856, Jul. 8, 1997, Delivery systems for hydrophobic drugs; Jonathan Ernest Lacy, et al., 424/455, 456; 514/784, 785, 786, 937, 975 [IMAGE AVAILABLE]

4. 5,449,679, Sep. 12, 1995, Process and products for reducing biological fluid levels of a lipid soluble waste; Robert J. Leonard, 514/310; 128/898; 424/422, 424, 426; 514/824; 604/5, 19 [IMAGE AVAILABLE]

5. 5,446,070, Aug. 29, 1995, Compositions and methods for topical administration of pharmaceutically active agents; Juan A. Mantelle, 514/772.6; 424/485, 486, 487, 488; 514/781, 782 [IMAGE AVAILABLE]

=> d 1-5 kwic

US PAT NO: 5,786,344 [IMAGE AVAILABLE]

L4: 1 of 5

SUMMARY:

BSUM(44)

Further . . . acids, which compounds often function as hypolipidemic compounds (Boiteux-Antoine et al., 1989). Suitable aryloxy-carboxylic and

arylcarboxylic acids include clofibrate, ciprofibrate, **fenofibrate**, bezafibrate, gemfibrozil, tiadenol, probucol and the active compound 2-phenylpropionic acid (Magdalou et al., 1993; Fournel et al., 1985; Boiteux-Antoine et. . . .

SUMMARY:

BSUM(70)

Also biliary transport protein activity. Such compositions may include the first camptothecin drug or drugs in combination with Oltipraz, clofibrate, ciprofibrate, **fenofibrate**, bezafibrate, gemfibrozil, tiadenol, probucol, phenobarbital, DILANTIN.TM., clonazepam, clotrimazole, buthionine sulfoximine (BSO), cyclophosphamide, ifosfamide, a retinoic acid, a corticosteroid, an oral. . . .

DETDESC:

DETD(83)

D. **Fenofibrate**

DETDESC:

DETD(84)

A related compound, **fenofibrate**, is widely prescribed in Europe. The usual dosage is 100 mg orally after each meal. Administration of the drug with. . . .

DETDESC:

DETD(86)

The structural formulas of clofibrate and the related fibric acid derivatives are shown in Table 4. Gemfibrozil, **fenofibrate**, bezafibrate, and ciprofibrate all are more potent than clofibrate and can be used in lower doses.

DETDESC:

DETD(447)

Fournel et al., "Structure-dependent induction of bilirubin glucuronidation and **lauric** acid 12-hydroxylation by arylcarboxylic acids chemically related to clofibrate," Biochimica et Biophysica Acta, 842:202-213, 1985.

CLAIMS:

CLMS(9)

9. The method of claim 8, wherein said second agent is clofibrate, ciprofibrate, **fenofibrate**, bezafibrate, gemfibrazol, tiadenol or probucol.

US PAT NO: 5,719,197 [IMAGE AVAILABLE]

L4: 2 of 5

SUMMARY:

BSUM(33)

The . . . polypropylene glycol, sorbitol, ethylene glycol, and the like. Other suitable solvents include fatty acids such as oleic acid, linoleic acid, **capric** acid and the like, as well as fatty esters or alcohols. Further suitable solvents include other non-toxic, non-volatile solvents commonly. . .

DETDESC:

DETD(92)

Aryloxyalkanoic Acid Derivatives such as Beclorbrate, Bazafibrate, Binifibrate, Ciprofibrate, Clinofibrate, Clofibrate, Clofibric Acid, Etonfibrate, **Fenofibrate**, Gemfibrozil, Nicofibrate, Pirifibrate, Ronifibrate, Simfibrate, Theofibrate

US PAT NO: 5,645,856 [IMAGE AVAILABLE]

L4: 3 of 5

DRAWING DESC:

DRWD(4)

1. Fatty acids e.g. oleic acid, linoleic acid, linolenic acid, stearic acid, myristic acid, **lauric** acid, palmitic acid, **capric** acid and **caprylic** acid. Oleic acid is preferred.

DRAWING DESC:

DRWD(7)

The preferred members of this class of lipophilic surfactants are the partial glycerides of **capric/caprylic** acid e.g. Imwitor 988 and Imwitor 742.

DRAWING DESC:

DRWD(8)

3. . . . lactic, citric and/or tartaric esters of mono- and/or di-glycerides of fatty acids
e.g. _____

Myvacet 9-45 (distilled acetylated monoglycerides)
Miglyol 829 (**caprylic/capric** diglyceryl succinate)
Myverol SMG (mono/di-succinylated monoglycerides)
Imwitor 370 (glyceryl stearate citrate)
Imwitor 375 (glyceryl monostearate/citrate/lactate)
Crodatem T22 (Diacetyl tartaric esters. . .)

DRAWING DESC:

DRWD(15)

7. . . . ethoxylates--formed by reacting ethylene oxide with fatty acids or glycerol esters of fatty acids (HLB<10)
e.g.

Crodet 04 (polyoxyethylene (4) **lauric** acid)
Cithrol 2MS (polyoxyethylene (2) stearic acid)
Marlosol 183 (polyoxyethylene (3) stearic acid)
Marlowet G12DO (glyceryl 12 EO dioleate) and. . .

DRAWING DESC:

DRWD(60)

As . . . also surprisingly discovered that one class of hydrophilic surfactants, namely the transesterification products of polyoxyethylene glycol with glycerol esters of **capric** and **caprylic** acids, does not substantially inhibit the in vivo lipolysis of digestible oils. Accordingly, with this class of hydrophilic surfactants there. . .

DRAWING DESC:

DRWD(63)

(b) a transesterification product of polyoxy-ethylene glycol with glycerol esters of **capric** and/or **caprylic** acids as hydrophilic surfactant, and

DRAWING DESC:

DRWD(65)

Examples . . . used in this aspect of the present invention are:

Labrasol (glyceryl caprylate/caprate and PEG-8 caprylate/caprate) and
Softigen 767 (PEG-6 **caprylic/capric** glycerides)

DRAWING DESC:

DRWD(73)

Further . . . those containing saturated C.sub.6 -C.sub.12 fatty

acids, for instance fractionated vegetable oils e.g. fractionated coconut oils. Specific examples of useful **capric** and/or **caprylic** triglyceride oils include: Miglyol 810, Miglyol 812, Neobee M5, Neobee 0, Captex 300, Captex 355 and Captex 8000. The "Miglyol". . .

DRAWING DESC:

DRWD(106)

Lipid regulating agents: bezafibrate, clofibrate, **fenofibrate**, gemfibrozil, probucol.

DRAWING DESC:

DRWD(121)

In . . . much higher solubilising power for hydrophobic drugs than pure bile salt micelles. This is illustrated with the hydrophobic antihyperlipoproteinemic drug **fenofibrate** which we have shown is >20 times more soluble in mixed micelles than simple bile salt micelles.

DETDESC:

DETD(26)

Experiment (iii) 15 mM crude ox gallbladder bile+500 mg of medium chain lipolytic products (137 mg **capric** acid, 98 mg glyceryl monocaprate, 151 mg **caprylic** acid and 114 mg glyceryl monocaprylate)

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The drugs investigated using this method were: Carbamazepine, griseofulvin, **fenofibrate** and probucol.

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Griseofulvin

Fenofibrate

Probucol

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ii	1.1	4.6	38.5	>71.0
iii	2.6	7.4	188.5	>320.0

DETDESC:

DETD(42)

pH 6.50 tris-maleate buffer solution+15mM ox bile+medium chain lipolytic products viz 53% by weight of **caprylic** acid-monocaprylate (2:1 molar ratio) and 47% by weight of **capric** acid-monocaprate (2:1 molar ratio)

DETDESC:

DETD(57)

80 . . .

	275 mg
Priolene	275 mg
Soybean Oil	
	185 mg
Triacetin	
	185 mg
Fenofibrate	
	80 mg

CLAIMS:

CLMS(11)

11. . . . according to claim 2, wherein said hydrophilic surfactant component comprises a transesterification product of polyethylene glycol with glycerol esters of **capric** and **caprylic** acids.

US PAT NO: 5,449,679 [IMAGE AVAILABLE]

L4: 4 of 5

SUMMARY:

BSUM(7)

Several . . . Other agents that have met with varying degrees of success with respect to reducing plasma LDL levels include gemifibrozil, clofibrate, **fenofibrate**, cholestyramine, colestipol and nicotinic acid. (See, e.g., U.S. Pat. No. 5,112,827, issued to Saunders, Jr. et al., the contents of. . .

DETDESC:

DETD(28)

According . . . materials include cholesteryl acetate and other

.cholesteryl esters that contain fatty acids having between two and twenty-four carbons, such as **lauric** acid, myristic acid, palmitic acid, stearic acid, glucuronic acid). Exemplary biodegradable, lipid substances, as well as three exemplary processes by. . .

US PAT NO: 5,446,070 [IMAGE AVAILABLE]

L4: 5 of 5

DETDESC:

DETD(9)

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10

=> s l1 and (polyglycerol or polyglyceryl?)

5 POLYGLYEROL

382 POLYGLYCERYL?

L5 1 L1 AND (POLYGLYEROL OR POLYGLYCERYL?)

=> d 1

1. 5,645,856, Jul. 8, 1997, Delivery systems for hydrophobic drugs;

Jonathan Ernest Lacy, et al., 424/455, 456; 514/784, 785, 786, 937, 975

[IMAGE AVAILABLE]

=> s l1 and ?fibrate?

1159 ?FIBRATE?
L2 1 L1 AND ?FIBRATE?

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[IMAGE AVAILABLE]

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US PAT NO: 5,645,856 [IMAGE AVAILABLE] L2: 1 of 1

DRAWING DESC:

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